International Application No. PCT/BE2004/000089

Attorney Docket: BOUW3001/JEK

LIST OF CURRENT CLAIMS

Claims 1-44 (Canceled)

- 45. (New) An in vitro method of generating insulin producing beta cells from a population comprising dedifferentiated exocrine pancreatic cells of a first mammal, said method comprising the steps of:
- a) providing a population comprising dedifferentiated exocrine pancreatic cells in a culture medium,
- b) adding one or more ligands of the gp130 receptor of a second mammal and/or adding one or more ligands of the EGF receptor of a third mammal to said culture medium,
- c) incubating said dedifferentiated exocrine pancreatic cells in said culture medium comprising said one or more ligands of the gp130 receptor and/or said one or more ligands of the EGF receptor.
- 46. (New) The method according to claim 45, wherein said ligand of said gp130 receptor is LIF.
- 47. (New) The method according to claim 45, wherein said ligand of said EGF receptor is EGF.
- 48. (New) The method according to claim 45, wherein the method further comprises the step of adding bFGF to said culture medium during step b).
- 49. (New) The method according to claim 45, wherein said medium is free from KGF or a gastrin/CCK receptor ligand.
- 50. (New) The method according to claim 45, wherein the population comprising dedifferentiated exocrine pancreatic cells is selected from the group

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consisting of duct cells, acinar cells and islet cells.

51. (New) The method according to claim 45, further comprising, prior to step a), a preliminary step of depleting said population from beta cells.

52 (New) A population of mammalian pancreatic cells comprising mammalian insulin producing beta cells obtainable by an in vitro method of generating insulin producing beta cells from a population comprising dedifferentiated exocrine pancreatic cells of a first mammal, said method comprising the steps of :

- a) providing a population comprising dedifferentiated exocrine pancreatic cells in a culture medium,
- b) adding one or more ligands of the gp130 receptor of a second mammal and/or adding one or more ligands of the EGF receptor of a third mammal to said culture medium,
- c) incubating said dedifferentiated exocrine pancreatic cells in said culture medium comprising said one or more ligands of the gp130 receptor and/or said one or more ligands of the EGF receptor.
- 53. (New) The population of mammalian pancreatic cells according to claim 52, wherein said population comprises from about 5 to about 15 percent of insulin-positive cells.
- 54. (New) The population of mammalian pancreatic cells according to claim 52, wherein said cell population after exposure to 20 mM glucose for 4 hours at 37 °C in RPMI-1640 medium supplemented with 10% fetal bovine serum shows a more than 2 fold increase in insulin secretion when compared to the insulin secretion prior to said exposure to glucose.
- 55. (New) The population of mammalian pancreatic cells according to claim 52, being able to provide an insulin secretion of at least 10 ng/ml after exposure of said population to 20 mM glucose for 4 hours at 37 °C in RPMI-1640 medium

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supplemented with 10% fetal bovine.

- 56. (New) A pharmaceutical composition comprising a therapeutically active amount of a mammalian pancreatic cell population according to claim 52, and at least one pharmaceutically acceptable carrier.
- 57. (New) A method of prevention or treatment of diabetes type 1 or type 2 comprising administration of a therapeutically effective amount of a combination of a human or humanised ligand of a EGF receptor, and a human or humanised ligand of the gp130 receptor.
- 58. (New) A method of prevention or treatment of diabetes type 1 or type 2 comprising administration of a therapeutically effective amount of a human or humanised ligand of the gp130 receptor.
- 59. (New) The method of prevention or treatment according to claim 58, further comprising administration of a human or humanised ligand of a EGF receptor.
- 60. (New) The method of prevention or treatment according to claim 58, wherein said human or humanised ligand of the gp130 receptor is LIF.
- 61. (New) A population of mammalian pancreatic cells according to claim 52 being identifiable by an in vitro method for determining the degree of redifferentiation of a dedifferentiated mammalian pancreatic cells comprising the steps of determining one or more parameters selected from the group consisting of:
 - a) The presence of CK 20, CK 7 or CK 19,
 - b) the occurrence of binucleated cells,
 - c) the presence of insulin positive cells,
 - d) the presence of C-peptide, Pdx-1 and Glut-2,
 - e) the presence of gastrin CCKB receptor, PGP9.5 and notch-1 receptor, on said mammalian pancreatic cells.